EXPR[redacted] MAIL NO. EL 897860744US

19C

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Prior Application

Applicants	:	Michael Giesing et al.
Application No.	:	09/485,879
Filed	:	June 22, 2000
For	:	METHOD FOR THE CHARACTERIZATION OF DISSEMINATED AND MICROMETASTASIZED CANCER CELLS

Art Unit	:	1655
Docket No.	:	790076.401
Date	:	June 28, 2002

Box CPA
Commissioner for Patents
Washington, DC 20231

PRELIMINARY AMENDMENT

Commissioner for Patents:

Further to the Notice of Appeal submitted on November 29, 2001, please extend the period of time for response five months, to expire on June 29, 2002. Enclosed are a Petition for an Extension of Time and the requisite fee. Also enclosed please find a Request for Continued Prosecution Application under 37 C.F.R. §1.53(d) along with the fee set forth in §1.16.

In the Claims:

Please amend the claims as follows:

Please cancel claims 18-20, 23, and 40.

Please amend claims 21-22, 24, 27-30, 32 and 37 to read as follows:

21. (Amended) The method of claim 43 wherein the first and second cancer-specific nucleic acids are the same.

C1

22. (Amended) The method of claim 43 wherein the first and second cancer-specific nucleic acids are different.

24. (Amended) The method of any one of claims 54-56 wherein the RNA

C2

comprises mRNA.

27. (Amended) The method of any one of claims 54-56 wherein the DNA that is detected comprises genomic DNA selected from the group consisting of genomic DNA comprising a genomic mutation, genomic DNA comprising a gene that has undergone amplification, genomic DNA comprising a gene that has undergone loss of heterozygosity, genomic DNA comprising a translocated gene and genomic DNA comprising a gene polymorphism.

C3

28. (Amended) The method of any one of claims 54-56 wherein at least one nucleic acid that is detected comprises DNA, said DNA comprising genomic DNA selected from the group consisting of (i) the second cancer-specific nucleic acid and (ii) a cancer-associated nucleic acid that is present in at least one cancer cell in the second fraction.

29. (Amended) The method of any one of claims 54-56 wherein the DNA is genomic DNA that comprises all or a portion of an oncogene.

30. (Amended) The method of any one of claims 54-56 wherein the DNA is genomic DNA that comprises all or a portion of a tumor suppressor gene.

C4

32. (Amended) The method of any one of claims 41-43 wherein at least one nucleic acid selected from the group consisting of a (i) first cancer-associated nucleic acid and (ii) a second cancer-associated nucleic acid comprises a coding portion of a gene selected from

C4 the group consisting of a tissue-specific gene, a metastasis-associated gene, a steroid hormone receptor gene, a drug resistance gene, an immunomodulation gene, a cell proliferation gene and an apoptosis gene, or a complementary nucleic acid thereto.

C5 37. (Amended) The method of any one of claims 41-43 wherein the cancer cell is removed from the body fluid by a method selected from the group consisting of microfiltration, density gradient centrifugation and antigen-specific immunoadsorption.

Please add new claims 41-59 to read as follows:

C6 41. (New) A method for determining an increased risk for or presence of a disseminated cancer cell or a micrometastasizing cancer cell in a body fluid from a subject, comprising:

(a) dividing a plurality of cells into at least a first fraction and a second fraction, wherein each of the fractions comprises at least one cell and wherein the plurality of cells is from a body fluid of a subject known to have or suspected of being at risk for having a disseminated cancer cell or a micrometastasized cancer cell, and wherein the second fraction comprises at least one cell that has been removed from said body fluid according to a method for isolating cancer cells from non-cancer cells;

(b) detecting in the first fraction an absence or presence of at least one first nucleic acid selected from the group consisting of a first cancer-specific nucleic acid and a first cancer-associated nucleic acid; and

(c) detecting, in the second fraction, an absence or presence of at least one second nucleic acid selected from the group consisting of a second cancer-specific nucleic acid and a second cancer-associated nucleic acid, wherein said first and second cancer-specific nucleic acids are different, wherein said first and second cancer-associated nucleic acids are different, wherein the presence of said first nucleic acid in the first fraction and an increased or decreased presence of the second nucleic acid in said second fraction relative to the presence or absence of said second nucleic acid in a non-cancer cell from the subject indicate an increased risk for having a disseminated cancer cell or a micrometastasized cancer cell.

42. (New) A method for determining an increased risk for or presence of a disseminated cancer cell or a micrometastasizing cancer cell in a body fluid from a subject, comprising:

(a) dividing a plurality of cells into at least a first fraction and a second fraction, wherein each of the fractions comprises at least one cell and wherein the plurality of cells is from a body fluid of a subject known to have or suspected of being at risk for having a disseminated cancer cell or a micrometastasized cancer cell, and wherein the second fraction comprises at least one cell that has been removed from said body fluid according to a method for isolating cancer cells from non-cancer cells;

(b) detecting in the first fraction an absence or presence of at least one first cancer-specific nucleic acid; and

(c) detecting in the second fraction an absence or presence of at least one second cancer-specific nucleic acid, wherein said first and second cancer-specific nucleic acids are different, wherein the presence of said first cancer-specific nucleic acid in said first fraction and an increased or decreased presence of said second cancer-specific nucleic acid in said second fraction relative to the presence or absence of said second cancer-specific nucleic acid in a non-cancer cell from the subject indicate an increased risk for having a disseminated cancer cell or a micrometastasized cancer cell.

43. (New) A method for determining an increased risk for or presence of a disseminated cancer cell or a micrometastasizing cancer cell in a body fluid from a subject, comprising:

(a) dividing a plurality of cells into at least a first fraction and a second fraction, wherein each of the fractions comprises at least one cell and wherein the plurality of cells is from a body fluid of a subject known to have or suspected of being at risk for having a disseminated cancer cell or a micrometastasized cancer cell, and wherein the second fraction comprises at least one cell that has been removed from said body fluid according to a method for isolating cancer cells from non-cancer cells;

(b) detecting in the first fraction an absence or presence of at least one first cancer-specific nucleic acid;

(c) detecting in the second fraction an absence or presence of at least one second cancer-specific nucleic acid; and

(d) detecting an absence or presence of at least one cancer-associated nucleic acid in at least one sample selected from the group consisting of (i) the first fraction and (ii) the second fraction, wherein the presence of said first cancer-specific nucleic acid and of said cancer-associated nucleic acid in said first fraction and an increased or decreased presence of said second cancer-specific nucleic acid and of said second cancer-associated nucleic acid in said second fraction relative to the presence or absence of said second cancer-specific nucleic acid and of said second cancer-associated nucleic acid in a non-cancer cell from the subject indicate an increased risk for having a disseminated cancer cell or a micrometastasized cancer cell.

44. (New) The method of any one of claims 41-43 wherein a nucleic acid selected from the group consisting of (i) a first cancer-specific nucleic acid and (ii) a first cancer-associated nucleic acid comprises an organotypical gene, and wherein the presence of at least one of said first nucleic acids comprising an organotypical gene indicates the type of malignant disease from which the cancer cell is derived.

45. (New) The method of any one of claims 41-43 wherein a nucleic acid selected from the group consisting of (i) a first cancer-associated nucleic acid and (ii) a second cancer-associated nucleic acid comprises a metastasis-associated gene, and wherein the presence of said first cancer-associated nucleic acid comprising the metastasis-associated gene indicates an increased risk that a disseminated cancer cell has the ability to metastasize, and wherein an increased or decreased presence of said second cancer-associated nucleic acid comprising the metastasis-associated gene in said cancer cell relative to the presence or absence of said second cancer-associated nucleic acid comprising the metastasis-associated gene in a non-cancer cell from the subject indicates an increased risk that a disseminated cancer cell has the ability to metastasize.

46. (New) The method of claim 45 wherein the metastasis-associated gene encodes a gene product selected from the group consisting of an angiogenesis factor, a motility factor, a growth factor, a matrix degradation factor and an adhesion factor.

47. (New) The method of claim 46 wherein the matrix degradation factor is selected from the group consisting of a proteinase and a proteinase inhibitor.

48. (New) The method of claim 46 wherein the adhesion factor is an adherin.

49. (New) The method of claim 45 wherein the nucleic acid is selected from the group consisting of DNA and RNA.

50. (New) The method of claim 49 wherein the RNA comprises mRNA.

51. (New) The method of claim 50 wherein the mRNA encodes a gene product selected from the group consisting of bFGF, bFGF-R, VEGF, VEGF-R1, VEGF-R2, MMP2 and TIMP3.

52. (New) The method according to any one of claims 41-42 wherein steps (a) - (c) are performed before and after administering a candidate anticancer therapy to a subject known to have or suspected of being at risk for having a disseminated cancer cell or a micrometastasized cancer cell.

53. (New) The method according to claim 43 wherein steps (a) - (d) are performed before and after administering a candidate anticancer therapy to a subject known to have or suspected of being at risk for having a disseminated cancer cell or a micrometastasized cancer cell.

54. (New) The method of claim 41 wherein the first nucleic acid is RNA and wherein the second nucleic acid is selected from the group consisting of DNA and RNA.

55. (New) The method of claim 42 wherein the first cancer-specific nucleic acid is RNA and wherein the second cancer-specific nucleic acid is selected from the group consisting of DNA and RNA.

56. (New) The method of claim 43 wherein the first cancer-specific nucleic acid is selected from the group consisting of DNA and RNA, wherein the second cancer-specific nucleic acid is selected from the group consisting of DNA and RNA, and wherein the cancer-associated nucleic acid is selected from the group consisting of DNA and RNA.

57. (New) The method of claim 44 wherein the organotypical gene encodes an organotypical marker.

58. (New) The method of claim 44 wherein the first nucleic acid is RNA.

59. (New) The method of claim 58 wherein the RNA comprises mRNA.